

09/870729

Term	Documents
TWO.DWPI,EPAB,JPAB,USPT.	5134618
TWOES	0
TWOS.DWPI,EPAB,JPAB,USPT.	2161
TWOE.DWPI,EPAB,JPAB,USPT.	13
PRIMER\$1	0
PRIMER.DWPI,EPAB,JPAB,USPT.	68054
PRIMERA.DWPI,EPAB,JPAB,USPT.	36
PRIMERC.DWPI,EPAB,JPAB,USPT.	2
PRIMERD.DWPI,EPAB,JPAB,USPT.	2
PRIMERE.DWPI,EPAB,JPAB,USPT.	6
PRIMERF.DWPI,EPAB,JPAB,USPT.	1
(L2 AND (TWO NEAR5 PRIMER\$1)).USPT,JPAB,EPAB,DWPI.	8

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- 
- ☐ 1. [6323009](#). 28 Jun 00; 27 Nov 01. Multiply-primed amplification of nucleic acid sequences. Lasken; Roger S., et al. 435/91.1; 435/91.2. C12P019/34.
- 
- ☐ 2. [6291187](#). 24 May 00; 18 Sep 01. Poly-primed amplification of nucleic acid sequences. Kingsmore; Stephen, et al. 435/6; 435/91.1 435/91.2 536/23.1 536/24.3. C12Q001/68 C12P019/34 C12P021/04 C07H021/02 C07H021/04.
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- ☐ 3. [6117635](#). 11 Apr 97; 12 Sep 00. Nucleic acid amplification oligonucleotides with molecular energy transfer labels and methods based thereon. Nazarenko; Irina A., et al. 435/6; 435/91.2 536/22.1 536/24.33 536/25.32. C12Q001/68 C12P019/34 C07H021/04 C07H021/00.
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- ☐ 4. [6090552](#). 11 Jul 97; 18 Jul 00. Nucleic acid amplification oligonucleotides with molecular energy transfer labels and methods based thereon. Nazarenko; Irina A., et al. 435/6; 435/91.2 536/24.3 536/24.32 536/24.33. C12Q001/68 C12P019/34 C07H021/04 C12N015/00.
- 
- ☐ 5. [5866336](#). 03 Jan 97; 02 Feb 99. Nucleic acid amplification oligonucleotides with molecular energy transfer labels and methods based thereon. Nazarenko; Irina A., et al. 435/6; 435/91.2 536/22.1 536/24.3 536/25.32. C12Q001/68 C12P017/34 C07H021/06 C07H021/00.
- 
- ☐ 6. [5807669](#). 26 Apr 94; 15 Sep 98. Process for the detection of reverse transcriptase. Schupbach; Jorg, et al. 435/4; 435/5 435/6 435/91.2 536/23.1 536/24.3. C12Q001/00 C12Q001/70 C12Q001/68 C07H021/02.
- 
- ☐ 7. [5635617](#). 26 Apr 94; 03 Jun 97. Methods and compositions comprising the agfA gene for detection of Salmonella. Doran; James L., et al. 536/23.7; 536/23.1. C07H021/02 C07H021/04.
- 
- ☐ 8. [5314809](#). 10 Mar 93; 24 May 94. Methods for nucleic acid amplification. Erlich; Henry A., et al. 435/91.2; 435/6 536/24.3. C12Q001/68 C12P019/34 C07H015/12.
- 

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Generate Collection

L3: Entry 1 of 8

File: USPT

Nov 27, 2001

DOCUMENT-IDENTIFIER: US 6323009 B1

TITLE: Multiply-primed amplification of nucleic acid sequences

Brief Summary Paragraph Right (6):

The methods of the present invention (referred to herein as Multiply-Primed Rolling Circle Amplification--MPRCA) avoid such disadvantages by employing procedures that improve on the sensitivity of linear rolling circle amplification by using multiple primers for the amplification of individual target circles. The present invention has the advantage of generating multiple tandem-sequence DNA (TS-DNA) copies from each circular target DNA molecule. In addition, MPRCA has the advantages that in some embodiments the sequence of the circular target DNA molecule may be unknown while the circular target DNA molecule may be single-stranded (ssDNA) or double-stranded (dsDNA or duplex DNA). Another advantage of some embodiments of the present invention is that the amplification of single-stranded or double-stranded circular target DNA molecules may be carried out isothermally and/or at ambient temperatures. Other advantages include being highly useful in new applications of rolling circle amplification, low cost, sensitivity to low concentration of target circle, flexibility, especially in the use of detection reagents, and low risk of contamination.

Brief Summary Paragraph Right (14):

In separate embodiments of the foregoing methods, the use of multiple primers is achieved in several different ways. It is achieved by using two or more specific primers that anneal to different sequences on the circle, or by having one given primer anneal to a sequence repeated at two or more separate locations on the circle, or by using random or degenerate primers, which can anneal to many locations on the circle. Degenerate refers to an oligonucleotide in which one or more of the nucleotide positions is occupied by more than one base, i.e., a mixture of oligonucleotides of defined length in which one or more positions of an individual member of the mixture is occupied by a base selected at random from among more than one possibilities for that position. Such collections of oligonucleotides are readily synthesized using standard oligonucleotide synthesis instruments and software. Random refers to an oligonucleotide in which each of the nucleotide positions is occupied by a base selected at random from among a complete set of possibilities, but commonly limited to the four nucleosides, dAMP, dCMP, dGMP, or dTMP.

Detailed Description Paragraph Right (11):

A sample embodiment of the present invention, using multiple (here, three) primers for each amplification target circle (ATC), is shown in FIG. 1. Oligonucleotide primers (each about 20-50 bases in length and shown in A) with regions complementary to separate segments of an amplification target circle hybridize specifically to the amplification target circle (shown in B). C shows the results of addition of dNTPs, DNA polymerase, etc., to the hybridized structures of B, whereby the 3'-end of each primer is extended. Extension of each product continues, with the DNA polymerase displacing the DNA synthesized by the adjacent enzyme. Oligonucleotide primers may optionally contain a region or sequence of nucleotides at the 5' end of said primers, which region or sequence of nucleotides is non-complementary to the ATC if such a non-complementary region or sequence of nucleotides is deemed useful for increasing the ability of the DNA polymerase to carry out strand-displacement DNA synthesis. In the specific embodiment shown here, one ATC interacts with 3 primers and 3 enzyme molecules to achieve 3 rounds of linear replication on the same amplification target circle template.

Detailed Description Paragraph Right (38):

Exonuclease-resistant primers useful in the methods disclosed herein may include modified nucleotides to make them resistant to exonuclease digestion. For example, a primer may possess one, two, three or four phosphorothioate linkages between

nucleotides at the 3' end of the primer.

Detailed Description Paragraph Right (40):

It may also be advantageous within the present invention to provide a means for attaching an ATC template to a solid support. To accomplish this, one need only attach a single oligonucleotide primer to a solid support for each of the ATCs to be amplified. Thus, in carrying out the processes of the present invention, a given ATC will be attached to multiple primers, only one of which needs itself to be tethered to some type of solid support. Often, it is advantageous that such a tethering primer be bipolar, thus having two 3'-ends whereby one such end serves to attach the primer to the support while the other can attach to the circle and provide a primer for amplification. None of the other multiple primers attached to the ATC need be themselves attached to any type of support. The bipolar tethering primer may be specific or random without drawback to the processes disclosed herein. Examples of such bipolar primers, and their preparation and use, are well known in the literature [see, for example, the disclosure of Lizardi et al (1998), supra].

Detailed Description Paragraph Right (87):

DNA samples were prepared as follows. A BAC-containing bacterial strain (Research Genetics) was streaked out and grown up as single colonies. A piece of polyethylene tubing (Intramedic, PE20, 1.09 mm outer diameter) was stabbed into a colony and the tubing was placed into a thermocycler tube (200 .mu.l) containing 10 .mu.l of buffer (20 mM Tris-HCl, pH 8.0, 150 mM KCl, 0.1 mM EDTA). Exonuclease-resistant, random hexamer primer (random hexamer modified to contain two thiophosphate linkages located closest to the 3' end of the oligonucleotide, 350 pmol) was added to each tube and the reactions were heated to 95.degree. C. for 3 minutes and cooled immediately to room temperature. In order to carry out RCA the reactions were brought to a final volume of 20 .mu.l containing final concentrations of 25 mM Tris-HCl, pH 7.5, 10 mM MgCl.sub.2, 75 mM KCl, 0.5 mM deoxyribonucleoside triphosphates, 0.03 units of yeast pyrophosphatase, and 2.0 units .phi.29 DNA polymerase.

CLAIMS:

10. The process of claim 1 wherein said multiple primers contain a region at the 5' end of said primers non-complementary to the ATC.

48. The process of claim 44 wherein each of said exonuclease-resistant primers contains at least two nucleotides making said primer resistant to exonuclease activity.

STN 09/870729

FILE 'HOME' ENTERED AT 15:41:38 ON 02 MAY 2002

=> file medline caplus biosis  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.42	0.42

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:42:31 ON 02 MAY 2002

FILE 'CAPLUS' ENTERED AT 15:42:31 ON 02 MAY 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE 'BIOSIS' ENTERED AT 15:42:31 ON 02 MAY 2002  
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=> s detect?(10a) contaminat?

L1 11752 DETECT?(10A) CONTAMINAT?

=> s l1 and (primer# (10a) non-complementay)

L2 0 L1 AND (PRIMER# (10A) NON-COMPLEMENTAY)

=> s l1 and primer# and non-complementary

L3 0 L1 AND PRIMER# AND NON-COMPLEMENTARY

=> s l1 and primer#

L4 682 L1 AND PRIMER#

=> s l4 and non-complementary

L5 0 L4 AND NON-COMPLEMENTARY

=> s l1 and (primer#(10a)two(10a)region#)

L6 7 L1 AND (PRIMER#(10A) TWO(10A) REGION#)

=> s l6 and complementary

L7 0 L6 AND COMPLEMENTARY

=> dup rem l6

PROCESSING COMPLETED FOR L6

L8 3 DUP REM L6 (4 DUPLICATES REMOVED)

=> d l8 1-3 bib ab

L8 ANSWER 1 OF 3 MEDLINE DUPLICATE 1  
AN 1999004755 MEDLINE  
DN 99004755 PubMed ID: 9790095  
TI Detection of Epstein-Barr virus (EBV) DNA and antigens in oral mucosa of renal transplant patients without clinical evidence of oral hairy leukoplakia (OHL).  
AU Ammatuna P; Capone F; Giambelluca D; Pizzo I; D'Alia G; Margiotta V  
CS Department of Hygiene and Microbiology, University of Palermo, Italy.  
SO JOURNAL OF ORAL PATHOLOGY AND MEDICINE, (1998 Oct) 27 (9) 420-7.  
Journal code: JRF; 8911934. ISSN: 0904-2512.  
CY Denmark  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Dental Journals; Priority Journals  
EM 199812  
ED Entered STN: 19990115  
Last Updated on STN: 19990115  
Entered Medline: 19981223  
AB The use of the polymerase chain reaction (PCR) to detect the presence of Epstein-Barr virus (EBV) DNA in oral mucosa in the absence of specific

lesions gives rise to the problem of identifying the real viral replication sites. To verify whether the **detection** of EBV is due to salivary **contamination** or its true replicative capacity in oral mucosa, saliva samples and exfoliated cells from four different oral mucosa sites were taken from 40 renal transplant patients and 20 normal subjects for examination by PCR using **two** pairs of **primers** specific for the BamHI-L and BamHI-K genomic **regions**. EBV-specific sequences were detected in one or more of the oral mucosa samples from 29 transplant patients (72.5%) and six healthy controls (30%), and in the saliva samples of 16 transplant patients (40%) and three healthy controls (15%). A total of 89 oral mucosa smears from 29 transplant patients, and 13 from healthy subjects, were EBV-positive. The positive samples were also investigated by means of in situ hybridization in order to confirm the intracellular presence of the viral genome, and by means of immunofluorescence testing with monoclonal antibodies to assess the possible expression of viral antigens. Hybridization with the EBV-specific probe was observed in 40/ 89 and 2/13 samples, respectively. Latent antigens (with or without lytic antigens) were detected in only 23 of the 40 samples (collected from eight different transplant patients) that were positive by in situ hybridization. Our data show that EBV is more frequently present in the oral mucosa of immunodeficient patients (where it can efficiently replicate) than in normal subjects.

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
 AN 1995:19596 CAPLUS  
 DN 122:231864  
 TI Detection of mycoplasmas in cell cultures by using two-step polymerase chain reaction  
 AU Wei, Hongmei; Yuan, Zenglin; Chen, Tianshou  
 CS Natl. Inst. Control Pharm. Biol. Prod., Beijing, 100050, Peop. Rep. China  
 SO Zhonghua Weishengwuxue He Mianyixue Zazhi (1994), 14(2), 131-4  
 CODEN: ZWMZDP; ISSN: 0254-5101  
 DT Journal  
 LA Chinese  
 AB

Two-step PCR has been applied to **detect** the **contamination** of Mycoplasmas in the cell cultures. **Two** sets of universal **primers** were selected from the conserved **regions** between 16S/23S intergenic spaces of these Mycoplasma species. The first PCR produced fragments of 360 to 500 bp, the second PCR products were from 140 to 220 bp. The test showed that the two-step PCR is more sensitive in that it could detect 9 species of Mycoplasmas, compared with the direct culture test that was able to detect 5 cell cultures pos. from 17 samples. We used the 1605 Air thermo-cycler, for shortening the amplification time from several hours to 20 min for 30 cycles, lessening the reaction vol. to 10 .mu.L, and increasing work efficiency.

L8 ANSWER 3 OF 3 MEDLINE DUPLICATE 3  
 AN 91157406 MEDLINE  
 DN 91157406 PubMed ID: 2293461  
 TI Absence of HIV DNA sequences in seronegative polytransfused thalassemic patients.  
 AU Lefrere J J; de Montalembert M; Mariotti M; Girot R; Salmon C; Rouger P; Rey J  
 CS Institut National de Transfusion Sanguine, Paris, France.  
 SO VOX SANGUINIS, (1990) 59 (4) 218-21.  
 Journal code: XLI; 0413606. ISSN: 0042-9007.  
 CY Switzerland  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199104  
 ED Entered STN: 19910428

Last Updated on STN: 19970203

Entered Medline: 19910411

AB The risk of infection with human immunodeficiency virus (HIV) by transfusion is not totally eliminated, since **contaminated** blood given before seroconversion to HIV is not **detected** on the actual biological screening. We used the polymerase chain reaction (PCR) assay (with one **primer** pair in the gag **region** and **two** in the pol **region**) to detect HIV DNA sequences in 30 seronegative polytransfused thalassemic patients and in 60 seropositive individuals (used as positive controls). We did not observe PCR-positive HIV-antibody-negative results in seronegative polytransfused patients.

=> d l8 2 kwic

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

AB Two-step PCR has been applied to **detect** the **contamination** of Mycoplasmas in the cell cultures. **Two** sets of universal **primers** were selected from the conserved **regions** between 16S/23S intergenic spaces of these Mycoplasma species. The first PCR produced fragments of 360 to 500 bp, the second.

FILE 'HOME' ENTERED AT 15:52:25 ON 02 MAY 2002

=> file medline caplus biosis  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FULL ESTIMATED COST

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FILE 'BIOSIS' ENTERED AT 15:52:48 ON 02 MAY 2002  
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=> s primer#(10a)non-complementary  
L1 41 PRIMER#(10A) NON-COMPLEMENTARY

=> s l1 and detect? and contaminat?  
L2 0 L1 AND DETECT? AND CONTAMINAT?

=> s l1 and detect?  
L3 6 L1 AND DETECT?

=> s l3 and contaminat/  
'CONTAMINAT/' IS NOT A VALID FIELD CODE  
'CONTAMINAT/' IS NOT A VALID FIELD CODE  
'CONTAMINAT/' IS NOT A VALID FIELD CODE  
For a list of field codes for the current file, enter "HELP SFIELDS"  
at an arrow prompt (=>).

=> s l3 and contaminat?  
L4 0 L3 AND CONTAMINAT?

=> s l1 and contaminat?  
L5 0 L1 AND CONTAMINAT?

=> s l1 and polymerase chain reaction#  
L6 8 L1 AND POLYMERASE CHAIN REACTION#

=> dup rem l6  
PROCESSING COMPLETED FOR L6  
L7 7 DUP REM L6 (1 DUPLICATE REMOVED)

=> d l7 1-7 bib ab kwic

L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS  
AN 2001:618192 CAPLUS  
DN 135:191254  
TI Multiplex DNA amplification using ligase chain reaction and amplification  
of ligation products using families of ligatabale probes  
IN Schouten, Johannes Petrus  
PA Neth.  
SO PCT Int. Appl., 158 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001061033	A2	20010823	WO 2001-EP1739	20010215
	WO 2001061033	A3	20020328		



W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1130113 A1 20010905 EP 2000-200506 20000215

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO

PRAI EP 2000-200506 A 20000215

AB Described is an improved multiplex ligation-dependent amplification method for detecting the presence and quantification of at least one specific single stranded target nucleic acid sequence in a sample using a plurality of probe sets of at least two probes, each of which includes a target specific region and a **non-complementary** region comprising a **primer** binding site. The probes belonging to the same set are ligated together when hybridized to the target nucleic acid sequence and amplified by a suitable primer set. By using a femtomolar amt. of the probes a large no. of different probe sets can be used to simultaneously detect and quantify a corresponding large no. of target sequences with high specificity. Use of the method in the detection of polymorphisms or mutations, in mRNA and library anal. and in the detection of genomic imprinting and DNA methylation is demonstrated.

AB Described is an improved multiplex ligation-dependent amplification method for detecting the presence and quantification of at least one specific single stranded target nucleic acid sequence in a sample using a plurality of probe sets of at least two probes, each of which includes a target specific region and a **non-complementary** region comprising a **primer** binding site. The probes belonging to the same set are ligated together when hybridized to the target nucleic acid sequence and amplified by a suitable primer set. By using a femtomolar amt. of the probes a large no. of different probe sets can be used to simultaneously detect and quantify a corresponding large no. of target sequences with high specificity. Use of the method in the detection of polymorphisms or mutations, in mRNA and library anal. and in the detection of genomic imprinting and DNA methylation is demonstrated.

IT PCR (**polymerase chain reaction**)  
 (for amplification of ligated probes; multiplex DNA amplification using ligase chain reaction and amplification of ligation products using families of ligatable probes)

L7 ANSWER 2 OF 7 MEDLINE

AN 1998335150 MEDLINE

DN 98335150 PubMed ID: 9670494

TI Simultaneous determination of STR polymorphism and a new nucleotide substitution in its flanking region at the CD4 locus.

AU Watanabe G; Umetsu K; Yuasa I; Suzuki T

CS Department of Forensic Medicine, Yamagata University School of Medicine, Japan.

SO JOURNAL OF FORENSIC SCIENCES, (1998 Jul) 43 (4) 733-7.

Journal code: I5Z; 0375370. ISSN: 0022-1198.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199808

ED Entered STN: 19980817

Last Updated on STN: 19980817

Entered Medline: 19980806

AB In the course of the investigation of a pentanucleotide repeat polymorphism at the human CD4 locus, a C-A transversion was found at the

position corresponding to the 3' end of the original forward primer presented by Edwards et al. (1). In the present study, the simultaneous determination of the new sequence polymorphism and the pentanucleotide repeat polymorphism at the CD4 locus was attempted. To achieve this purpose, we adopted amplified product length polymorphism (APLP) analysis and designed some new allele-specific forward **primers** tagged with **non-complementary** nucleotides differing in length. A total of 646 DNA samples from peripheral blood of Japanese, Chinese and German populations were investigated. Although the C-A transversion was restricted to CD4\*5, a new subtype allele with A and 5 repeats, designated CD4\*5A, was observed at polymorphic frequencies in the three populations. The simultaneous genotyping by APLP analysis resulted in dramatically increased heterozygosity and discriminating power of the human CD4 locus.

AB . . . . was attempted. To achieve this purpose, we adopted amplified product length polymorphism (APLP) analysis and designed some new allele-specific forward **primers** tagged with **non-complementary** nucleotides differing in length. A total of 646 DNA samples from peripheral blood of Japanese, Chinese and German populations were. . . .

CT . . . .

China

DNA Fingerprinting: MT, methods  
DNA Primers: CH, chemistry  
Germany  
Japan  
\*Minisatellite Repeats: GE, genetics  
Molecular Sequence Data  
\*Point Mutation  
**Polymerase Chain Reaction**  
\*Polymorphism (Genetics)

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS

AN 1997:746176 CAPLUS

DN 128:19361

TI Diagnostic detection and amplification of specific nucleic acid sequences in a two stage PCR using primers tailed with tag and detector domains

IN Whitcombe, David Mark; Little, Stephen; Brownie, Jannine

PA Zeneca Limited, UK; Whitcombe, David Mark; Little, Stephen; Brownie, Jannine

SO PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9742345	A1	19971113	WO 1997-GB1163	19970429
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	GB 2312747	A1	19971105	GB 1997-8581	19970429
	GB 2312747	B2	19980722		
	AU 9727049	A1	19971126	AU 1997-27049	19970429
	EP 896630	A1	19990217	EP 1997-920810	19970429
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000510337	T2	20000815	JP 1997-539623	19970429
	US 6270967	B1	20010807	US 1998-171982	19981029

PRAI GB 1996-9441 A 19960504  
WO 1997-GB1163 W 19970429

AB A two stage PCR method for the detection of diagnostic base sequences in sample nucleic acid uses diagnostic **primers** having **non-complementary** tails that include tag and detector regions. Use of tag and detector sequences minimizes problems such as false-positives arising from primer dimers. In the first stage, a pair of sequence-specific primers are used to amplify the target sequence in a limited no. of temp. cycles. The second stage uses the tail sequence as the primer to amplify the first stage reaction products. Use of primers for the tail sequences prevents the amplification of primer-dimer artifacts. Primers are designed to give the tag primer a higher m.p. than the sequence-specific primer. This allows the switch from amplification of the sequence-specific primer to the tag primer simply by switching the melting temp. in the PCR cycle. The method is of particular use in combination with the Amplification Refractory Mutation System (ARMS) for the detection of variant diagnostic base sequences against a background of normal diagnostic base sequences. The method is demonstrated by using it to detect a no. of known mutations in human genes.

AB A two stage PCR method for the detection of diagnostic base sequences in sample nucleic acid uses diagnostic **primers** having **non-complementary** tails that include tag and detector regions. Use of tag and detector sequences minimizes problems such as false-positives arising from primer dimers. In the first stage, a pair of sequence-specific primers are used to amplify the target sequence in a limited no. of temp. cycles. The second stage uses the tail sequence as the primer to amplify the first stage reaction products. Use of primers for the tail sequences prevents the amplification of primer-dimer artifacts. Primers are designed to give the tag primer a higher m.p. than the sequence-specific primer. This allows the switch from amplification of the sequence-specific primer to the tag primer simply by switching the melting temp. in the PCR cycle. The method is of particular use in combination with the Amplification Refractory Mutation System (ARMS) for the detection of variant diagnostic base sequences against a background of normal diagnostic base sequences. The method is demonstrated by using it to detect a no. of known mutations in human genes.

IT Cystic fibrosis  
Genotyping (method)  
PCR (**polymerase chain reaction**)  
(diagnostic detection and amplification of specific nucleic acid sequences in two stage PCR using primers tailed with tag and detector domains)

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS

AN 1997:803546 CAPLUS

DN 128:85147

TI PCR-based methods for preparation of polymers of micro genes

IN Shiba, Kiyotaka

PA Foundation for Scientific Technology Promotion, Japan

SO Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09322775	A2	19971216	JP 1996-147184	19960610
	CA 2205082	AA	19971210	CA 1997-2205082	19970609
	EP 812911	A2	19971217	EP 1997-109308	19970609
	EP 812911	A3	20010418		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

	US 6063595	A	20000516	US 1997-871809	19970609
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PRAI	JP 1996-147184	A	19960610		
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\* AB Disclosed is a PCR-based method for the prepn. of a micro gene, an oligonucleotide monomer, that subsequently polymd. into a high-mol. wt. DNA. The method employs a thermostable DNA polymerase that also exhibits 3'.fwdarw.5' exonuclease activity, and a pair of partially complementary oligonucleotide **primers** that also contain .gtoreq.1 **non-complementary** base at either/both 3'-termini. A polymd. DNA mol. capable of encoding approx. 16 kDa protein can be prepd. by this method. The method was demonstrated by using a mixt. of Taq polymerase and Pwo polymerase.

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IT PCR (**polymerase chain reaction**)  
(PCR-based methods for prepn. of polymers of micro genes)

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS

AN 1997:565169 CAPLUS

DN 127:258115

TI The elimination of primer-dimer accumulation in PCR

AU Brownie, Jannine; Shawcross, Susan; Theaker, Jane; Whitcombe, David; Ferrie, Richard; Newton, Clive; Little, Stephen

CS Zeneca Diagnostics, Gadbrook Park/Northwich/Cheshire, CW9 7RA, UK

SO Nucleic Acids Res. (1997), 25(16), 3235-3241

CODEN: NARHAD; ISSN: 0305-1048

PB Oxford University Press

DT Journal

LA English

AB We attempted to produce primer-dimers (PDs) from a variety of primers with differing types and extents of complementarity. Where PDs were produced they were cloned and sequenced. We were unable to produce detectable PDs either with individual primers alone or with similar sequence primers even if they had 3' complementarity. These observations led to the hypothesis that a system could be developed whereby the accumulation of PDs in a PCR may be eliminated. We demonstrate a method for the general suppression of PD formation that uses a sequence of addnl. nucleotides (a Tail) at the 5' ends of amplimers. Tailed amplimers are present at low concn. and only participate during early cycles of PCR. In subsequent PCR cycles, amplification is achieved using a single primer that has the same sequence as that of the Tail portion of the early cycle primers, which we refer to as a Tag. When products are small, as with PDs, there is a high local concn. of complementary sequences derived from the Tail. This favors the annealing of the complementary ends of a single strand produced by tailed primer interactions and gives rise to 'pan-handle' structures. The formation of these outcompetes the annealing of further Tag primers thereby preventing the accumulation of non-specific PD products. This aids the design of large multiplex reactions and provides a means of detecting specific amplicons directly in the reaction vessel by using an intercalating dye.

IT PCR (**polymerase chain reaction**)  
(HANDS (Homo-Tag Assisted Non-Dimer System); elimination of primer-dimer accumulation in PCR)

IT PCR (**polymerase chain reaction**)  
(multiplex; elimination of primer-dimer accumulation in PCR)

IT **Primers** (nucleic acid)  
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(tailed with **non-complementary** nucleic acid;  
elimination of **primer-dimer** accumulation in PCR)

L7 ANSWER 6 OF 7 MEDLINE DUPLICATE 1  
 AN 1998065265 MEDLINE  
 DN 98065265 PubMed ID: 9490618  
 TI [DNA polymerase mediated amplification of DNA fragments using primers with mismatches in the 3'-region].  
 Amplifikatsiya Tth-DNK-polimerazoi fragmentov DNK s praimerami, soderzhashchimi nekomplementarnye matritse nukleotidy v 3'-kontsevoi oblasti.  
 AU Ignatov K B; Kramarov V M; Uznadze O L; Miroshnikov A I  
 SO BIOORGANICHESKAIA KHIMIYA, (1997 Oct) 23 (10) 817-22.  
 Journal code: 928; 7804941. ISSN: 0132-3423.  
 CY RUSSIA: Russian Federation  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA Russian  
 FS Priority Journals  
 EM 199803  
 ED Entered STN: 19980312  
 Last Updated on STN: 19980312  
 Entered Medline: 19980303  
 AB The ability of three thermostable enzymes, Tth, Taq, and Klentaq DNA polymerases, to amplify DNA with primers containing mismatches in the 3'-terminal region was studied. It is shown that Tth polymerase, in contrast to the Taq and Klentaq enzymes, synthesizes equally well DNA with primers perfectly complementary to the template and with those containing mismatches next the 3'-end. The use of Tth DNA polymerase in the **polymerase chain reaction** was shown to result, in some cases, in a great number of additional, nonspecific DNA fragments as compared with Taq DNA polymerase. This may be due to the ability of Tth polymerase for DNA primer extension even if the 3'-terminal region of the **primer** contains nucleotides **non-complementary** to the template. Tth DNA polymerase and a Klentaq/Tth mixture (100:1) can be efficiently used in the amplification of DNA with degenerated primers and primers forming nonperfect duplexes with the template.  
 AB . . . complementary to the template and with those containing mismatches next the 3'-end. The use of Tth DNA polymerase in the **polymerase chain reaction** was shown to result, in some cases, in a great number of additional, nonspecific DNA fragments as compared with Taq. . . may be due to the ability of Tth polymerase for DNA primer extension even if the 3'-terminal region of the **primer** contains nucleotides **non-complementary** to the template. Tth DNA polymerase and a Klentaq/Tth mixture (100:1) can be efficiently used in the amplification of DNA. . .  
 CT . . . Comparative Study  
 \*DNA: BI, biosynthesis  
 DNA Polymerase I: CH, chemistry  
 DNA Primers  
 \*DNA-Directed DNA Polymerase: CH, chemistry  
 \*Exodeoxyribonucleases: CH, chemistry  
 \*Polymerase Chain Reaction  
 Templates  
 L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS  
 AN 1996:435266 CAPLUS  
 DN 125:78528  
 TI Multiplex ligations-dependent amplification using split probe reagents containing common primer binding sites  
 IN Carrino, John J.  
 PA Abbott Laboratories, USA  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1  
 PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9615271	A1	19960523	WO 1995-US14886	19951115
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 1994-344203		19941116		
AB	<p>A method of multiplex amplification features a plurality of split probe reagents (SPRs) each of which includes a target specific region defined by its 3' and 5' ends and, in <b>non-complementary</b> regions (NCRs), <b>primer</b> binding sites (PBSs) that are common to each split probe reagent. The 3' and 5' ends of each SPR are ligated together only when hybridized to its target-specific template strand but, once joined, all SPRs can be amplified by a common primer set in a PCR reaction. SPRs may be a continuous strand, the ends of which are ligatable to form a loop, or they may be distinct polynucleotide pairs. Specialized sequence segments may be employed to facilitate detection on the basis of specific sequences and/or length. Multiplex amplification is demonstrated for the detection of DNA from several human papillomavirus types using a single primer set and for the amplification of sections of the CFTR gene and detection of cystic fibrosis mutations.</p>				
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IT	<p>Genetic methods</p> <p><b>Polymerase chain reaction</b>  (multiplex ligations-dependent amplification; multiplex ligations-dependent amplification using split probe reagents contg. common primer binding sites)</p>				

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